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IS THE CAUSE OF POLIOMYELITIS ALWAYS THE SAME?

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It is generally believed at the present time that poliomyelitis is a communicable disease caused by a virus. However, this broad definition excludes other conditions to which the term "poliomyelitis" can also be applied. The meaning of the Greek words from which "poliomyelitis" is derived implies inflammation of the gray matter of the central nervous system regardless of the etiology. The modern definition, on the other hand, intimates that all cases of this disease are caused by a virus. This conclusion has originated from the fact that a "virus" has been isolated from a small number of cases during epidemics of this disease and it is concluded unjustifiably, therefore, that every case of poliomyelitis has the same cause. The restricted modern usage of the term "poliomyelitis" undoubtedly accounts for much of the confusion that exists today regarding this disease. From the laboratories and as a result of animal experiments unjustified inferences have emanated that are presumed to be applicable to all cases of poliomyelitis encountered in medical practice. Van Rooyen and Rhodes[1] (1948) make the following significant remark regarding this fact: "Theories of the pathogenesis of human poliomyelitis have resulted very largely from experimental work carried out on monkeys rather than on observations on the patient." It should be stressed at this point that physicians in practice have seen and will continue to see the majority of the cases of poliomyelitis.

The diagnosis of poliomyelitis is often very difficult and hazardous. Reports of the disease are often uncertain and frequently erroneous. Diagnosis is not based upon specific, critical tests, but usually upon the physician's judgement. During epidemics of poliomyelitis as many as fifty different diseases have been called "poliomyelitis" and patients have been sent to contagious disease hospitals where the diseases were sorted out.[2] In an epidemic of poliomyelitis in Tennessee, in 1941, there were erroneous and highly questionable diagnoses in a considerable proportion (over 30 per cent) of the cases, according to Lumsden.[3] Anderson[4] (1949) says; "Much of our uncertainty regarding poliomyelitis

has stemmed from an inability to define the disease with any degree of exactitude." "One never makes a diagnosis of any condition which one does not have in mind, and if one's mind is occupied with one disease, mistakes are certain to be made."[4] Many illnesses, some unrecognizable, occur during the season when poliomyelitis is prevalent. It is unjustifiable and unscientific to consider any of these to be a form of poliomyelitis until proved conclusively to be such by specific, scientific tests. Silverman[5] (1952) states regarding these unrecognizable cases that they can have only an academic interest as relating to the epidemiology of poliomyelitis.

Virus recovery tests are expensive, require time, are clinically impractical, and are carried out, therefore, in an insignificant number of cases of poliomyelitis during epidemics of that disease. Further, there is no correlation between the presence of antibodies in an individual and the occurrence of poliomyelitis. An appreciable number of patients fail to develop antibodies consequent to an attack or to show any increase later in the convalescent stage. Esquimos and Liberian negroes, where poliomyelitis is unknown to have occurred, have 90 to 100 per cent neutralization tests for their sera, according to Landon and Smith[6] (1934). Harmon and Harkins[7] (1937) presented evidence that poliomyelitis may develop in the presence of neutralizing antibodies. In a series of 183 patients convalescent from poliomyelitis, Landon[8] (1938) found that nearly 40 per cent showed no antibody. Burnet[9] (1939) concluded that poliomyelitis antibody is not the result of exposure to, or infection with, the virus of poliomyelitis.

Inconclusive evidence of a virus etiology in all cases of poliomyelitis is demonstrated by other facts. For example, in many cases where the diagnosis is made with certainty, virus recovery tests have proved to be negative. Even in fatal cases, it has not been possible in some cases to demonstrate a virus in the feces or in the spinal cord.

In the vast majority of cases of poliomyelitis, the criteria for diagnosis has depended almost entirely on the presence of an epidemic of the disease, neurological signs and the presence of a pleocytosis. However, ten per cent or more of the cases of poliomyelitis that are reported have normal spinal fluid cell counts and pleocytosis can occur, together with neurological signs, in

conditions other than infectious diseases. In the so-called abortive cases of poliomyelitis, there are no characteristic signs and the spinal fluid is usually normal; the diagnosis is made merely by implication.

During the past century many etiological factors have been suggested to explain poliomyelitis which may be classified in three principle groups: 1 Infectious, 2 Toxic, and 3 Metabolic.* Poliomyelitis investigations during the past forty years, however, have been confined almost exclusively to the infectious (virus) origin of the disease. The insistence that there is only one cause of poliomyelitis has obstructed investigation of all possibilities.[10, 11] In referring to the virus origin of this disease, Lumsden[12] (1938) states: "To some of us it does not appear to square with the facts obtained by epidemiological studies of the disease. It seems too elastic, too restful."

In view of the fact that the vast majority of the cases of poliomyelitis occuring during an epidemic of this disease are not subjected to viral recovery studies or any other accurate specific scientific test, but rather conclusions are based on the supposition of a virus infection, it is pertinent that we critically examine other causal factors that may produce the disease. "Poliomyelitis" is in fact, as will be shown, a collective name for a symptom complex which is produced under different circumstances by different causes.. Unfortunately, the general impression has been that it can be caused only by a virus. In the present state of uncertain and incomplete knowledge a study of the plural etiology of poliomyelitis should be fruitful.

Lovett[13] (1908), in reporting the 1907 epidemic of infantile paralysis in Massachusetts, said that it may be simply the clinical expression of the reaction of the spinal cord to one of several causes, of which infection may be one. Flexner[14] (1910) also suggested a possible plurality of causes of poliomyelitis. Still[15] (1915) raised the important question of plurality of causes when he asked: "May the lesion result from many different causes, infective and otherwise?" He pointed out that the clinical course and apparent exciting causes of some of the sporadic cases at least suggest the possibility that similar pathological changes may be due to dissimilar causes.

*The metabolic cause of poliomyelitis has been described by Huffman[17] (1911); Helms[18] (1941); and McCormick[19, 20] (1942, 1943, 1944, 1950).

Only by exercising a broad view shall we be able to extend and amplify our present ideas and eventually correlate the symptom-complex with the actual causes. Taylor[16] (1902) stated significantly concerning poliomyelitis: "Its final place must be determined by a study of its cause or causes, as related to various other degenerations and inflammations of the nervous system."

TOXIC CAUSES OF POLIOMYELITIS

Many reports have appeared in the medical literature of poliomyelitis following poisoning by organic and inorganic poisons; these have been reviewed by the writer.[10, 24-32] In the present report the occurrence of poliomyelitis as a result of bacterial toxins and as a complication or sequel of infectious diseases will be considered primarily.

Many of the older writers noted the supervention of poliomyelitis during the acute stage of the infectious or febrile diseases or during convalescence therefrom. Medin,[33] Strümpel,[34] as well as Zuppert,[35] found that many cases of poliomyelitis occurred in connection with the infectious diseases, including measles, scarlet fever and typhoid fever. Bartholow[36] (1887) states that cases frequently occur during the course or convalescence from the exanthemata and other acute febrile affections and a causal relation is considered to exist. Bassette[37] (1892) reported a series of eighteen cases of post-infectious paralytic affections and reviewed the literature on the subject. Some of her cases showed the occurrence of either neuritis alone, or poliomylitis alone, or both of these diseases conjointly, during or following measles, scarlet fever, diphtheria, whooping cough, mumps, etc. Caverly[38] (1894), in describing an epidemic of poliomyelitis in Vermont in 1894, stated that physicians practicing in the epidemic area at the time of the epidemic noted that the usual diseases of children were accompanied with exaggerated nervous symptoms. Headache, convulsions and delirium were common. Roberts[39] (1894), writing on poliomyelitis, states that it sometimes follows one of the acute exanthemata or other febrile diseases. Bruns and Windsheid[40] (1897), noting the induced disease of the spinal cord caused in experimental animals by a number of organisms, say that it is probable that a great number of disease germs have the power to produce poliomyelitis anterior. Holt[41] (1897) found that

12 per cent of a total of 566 cases of poliomyelitis came on as a sequel of some acute disease, notably diarrhea, scarlet fever, typhoid fever, whooping cough and vaccination. Hoch[42] (1905) says: "There is sufficient evidence at hand to consider the disease as a rule of an infectious nature, however, not depending upon a specific micro-organism but resulting from bacterial infections of various kinds, and at times from other poisons." Cotton[43] (1906) states: "It is known to follow or to complicate acute infectious diseases, such as measles, scarlatina and typhoid fever." Oppenheim[44] (1908) stated: "It is admitted that an attack may follow in the wake of infectious diseases, such as measles, scarlet fever and whooping cough; the disease has occasionally developed in connection with vaccination." Claud[45] (1911), stated as a result of his observations, that classical poliomyelitis is probably the result of diverse infectious agents. Chapin and Pisek[46] (1919) point out that poliomyelitis may be seen in connection with certain infectious fevers, such as scarlatina and typhoid fever. Pritchard[47] (1924) states that poliomyelitis is often a sequel of the febrile infections of childhood, especially scarlet fever, measles and diphtheria. Lumsden[1] (1941) noted an increased incidence of smallpox in the same counties scattered throughout Tennessee which coincided with an epidemic of poliomyelitis in the same districts. He also pointed out that there was a markedly higher morbidity and mortality from diphtheria in children under five years of age in the same localities. Vaquez Lapuente[48] (1943) reported that paralysis of the same extent and degree is caused by poliomyelitis or any infection. In 97 of 100 children, paralysis followed typical poliomyelitis in 17 cases; measles in 28 cases; and various other general infections in 52 cases. Piszcek[49] (1952) pointed out that in 1943, in Cook County, there were 1,262 poliomyelitis cases with 108 deaths. At the same time an epidemic of diphtheria was prevailing in Chicago.

It is not surprising that such reports as the above should have appeared in the medical literature because the fundamental action of a disease producing organism is dependent on the toxin that it elaborates rather than on the organism itself. Putnam[50] (1895) states regarding this fact: "It has been made pretty certain that the signs we think of as characteristic in the nervous affections following infectious processes are due far more to the toxic sub-

stances which are developed in the course of bacterial action than to the micro-organisms." He states further: "The prostrating influence of the original struggle, though it may end in the apparent defeat of the infective agent, is liable to search the hidden weaknesses of the nervous system and to lay it at the mercy of morbid agencies with which it would otherwise have been able to cope successfully."

Experiments with animals indicate that by using diverse organisms non-specific toxins can cause poliomyelitis. Oppenheim[44] (1908) states regarding these experiments: "Of recent years, by experimental introduction into animals of micro-organisms such as B. typhosus, B. influenza, B. diphtheriae or its toxin and also B. coli, anatomical changes in the spinal cord have been successfully produced, which, in their localization and nature, call to mind those of acute poliomyelitis." Lovett[13] (1908) makes a similar statement. He says: "The injection experiments prove that certain metallic poisons, bacteria and toxins have a selective action on the motor cells of the anterior cornua when present in the general circulation; that the paralysis of this type may be largely unilateral; that the posterior limbs are always more affected than the anterior; and that the lesions in the cord in such cases do not differ from those in anterior poliomyelitis."

The streptococcus has been the most intensively studied and the most frequently mentioned bacterium capable of producing poliomyelitis. Roger[51] (1891) injected rabbits intravenously with streptococci and noted, on examination of the nervous system, swelling and vascular degeneration of the anterior horn cells with atrophy of their nuclei. Bourges[52] (1893) inoculated animals subcutaneously and intravenously with erysipelas organisms, and these animals developed paraplegia, sphincter paralysis and muscular atrophy. Microscopical examination of the nervous system revealed vessel changes, cellular exudations, especially into the gray matter, and degeneration of the ganglion cells. Vidal and Bezancon[53] (1895) investigated the production of myelitis by means of streptococci injections. The animal used for the experiments was the rabbit. A total of 116 animals were injected with streptococci taken from 89 different sources and endowed with varying degrees of virulence. Of the 116 inoculations, seven animals, or six per cent, later developed paralytic symptoms. At autopsy,

degenerative lesions were found microscopically in both the gray and white matter. The gray matter throughout the cords was more or less affected, but especially in the lumbar enlargement. The ganglion cells of the anterior horns showed marked degenerative changes up to complete destruction. Bacteriological examinations of the rabbits' cords did not demonstrate the presence of streptococci, whereas, they were found at times in the viscera and blood. The legitimate conclusion was reached that the observed lesion was produced by soluble toxins and not by actual bacterial action.

A considerable amount of research work in the production of poliomyelitis with the streptococcus has been done in recent years, chiefly by Rosenow.[54] Although Rosenow and others have been able to demonstrate lesions characteristic of poliomyelitis in their studies, the objection to this work is the fact that they have considered the streptococcus to be the only cause of poliomyelitis.

The cases of poliomyelitis which have followed the injection of penicillin during epidemics of poliomyelitis in recent years could obviously be the result of the toxins of the streptococcus and other organisms rather than of the injection itself. Penicillin is bacteriostatic, not antitoxic. It is a well-known fact that the administration of penicillin in upper respiratory tract infections will be followed in some cases by sequelae despite the clearance of the original infection. This fact is illustrated by the development of acute glomerular nephritis* following scarlet fever and the rheumatic manifestations following streptococcus infections.

According to Gowers[55] (1888) limited atrophic paralysis sometimes occurs in typhoid fever, especially during convalescence, and he believes that in some cases the lesion is acute anterior poliomyelitis. Gumpertz[56] (1900), Lepine[57] (1903) and others have reported the appearance of poliomyelitis during the course of typhoid fever. Osler and McCrae[58] (1923) point out in their textbook, under complications of typhoid fever, that poliomyelitis may occure with the symptoms of acute ascending paralysis and prove fatal in a few days. "More frequently," they state, "it is less acute, and causes either a paraplegia or a limited atrophic paralysis of one arm or leg."

Vincent[59] (1883) used typhoid bacilli for his injection material in experiments on animals. He found in addition to degeneration

*Silverman[8] (1952) reported a case, a boy 16 years of age, with glomerular nephritis followed in four days by poliomyelitis.

of the anterior horn cells some proliferation of the neuroglia. Alajonine et al.[60] (1928) reported a case of poliomyelitis in a patient following antityphoid vaccination.

Gilbert and Lion[61] (1892) produced poliomyelitis in experimental animals with the streptococcus and Thoinet and Masselin[62] (1894) with the colon bacillus. Marinesco[63] (1900) produced lesions analogous to those of human poliomyelitis with the influenza bacillus, as well as with the streptococcus. Klingman[64] (1911) reported a case of anterior poliomyelitis caused by an acute gonorrheal infection and Oppenheim[44] saw one case of poliomyelitis preceded by a severe gonorrhea. Syphilitic acute anterior poliomyelitis has been described by a number of writers.[65-70]

In diphtheritic paralysis, as a result of toxins, the nervous system is involved both centrally and peripherally, that is, both the anterior horn cells and the peripheral nerve trunks are affected. Diphtheritic paralysis is usually not seen until the acute stage is passed and more often during convalescence. Bassette[37] reported a case of multiple neuritis and poliomyelitis after diphtheria in a four-year-old child. According to the experience of Mirabell[71] (1934), diphtheria may reproduce so thoroughly poliomyelitis in its paralysis, meningeal features, motor and sensory disturbances that a differential diagnosis is not always possible. Welch and Schamberg[72] (1905) point out that there are instances reported in which paralysis has occurred in persons who, presumably, were affected with the diphtheria poisons without having exhibited any of the ordinary symptoms of the disease.

Endriquez and Hallion[73] (1894) found that the toxins of diphtheria when injected beneath the skin of dogs, if the dose is not too large, may cause intense congestion of the gray matter of the cord, with hemorrhages and foci of inflammation, characterized by formative irritation of the neuroglia and destruction of the nerve elements. They also produced symptoms suggesting a similar process in the ape.

It is a well-known fact that in diphtheria antitoxin laboratories, guinea pigs used in routine tests of the strength of diphtheria toxins and antitoxins not infrequently develop paralysis. The animals which survive the inoculation for three weeks or longer suffer from paralysis during the third or fourth week. The paralysis may be slight, affecting but one limb, or somewhat em-

harrassing the respirations, or it may be severe and cause sudden or gradual death. Ehrlich[74] (1904) concluded that these paralytic phenomena resulted from the specific action of a portion of crude toxin which he designated *toxon*. Dryer and Madsen[75] had, however, worked with a toxin which, when injected in appropriate doses, caused such a paralysis. Jungeblut [76] (1934) observed marked lesions in the anterior horn cells of the spinal cord of monkeys dying with diphtheritic paralysis.

Lewis [77] (1906) injected 209 guinea pigs with diphtheria toxin-antitoxin containing one-tenth the standard antitoxic unit which neutralizes theoretically 10 minimal fatal doses. Nine, or four and three-tenths per cent, became paralyzed. Eight hundred and fifty-eight animals were injected with a toxin-antitoxin mixture containing the full standard antitoxic unit which neutralizes theoretically one hundred minimum fatal doses of diphtheria toxin. Two hundred and fifty-nine, or thirty and one-tenth per cent, of these animals became paralyzed.

The coexistence of influenza and poliomyelitis has been noted by a number of writers. Crookshank[78] (1920) traced the history of epidemics of influenza for about 450 years and pointed out the existence of poliomyelitis and polioencephalitis coinciding with epidemics of this disease. Goldflam[79] (1891) reported a case of polioencephalitis, superior and inferior and anterior poliomyelitis after influenza, with fatal termination. Bassette[37] points out that during and following influenza many forms of nervous diseases, functional and organic, have occurred, including neuritis, myelitis, cerebritis, meningitis and combinations of these inflamations. She reports a case, a boy, six years of age, who at the height of an epidemic of influenza had all the features corresponding to a localized poliomyelitis. She states that an unusual number of cases of juvenile paralysis were brought to the Polyclinic during the declining months of the epidemic of influenza. In 1899, Burckhard[80] reported a case of acute poliomyelitis after an attack of influenza in a 15-year-old girl. Lord[81] (1907), writing on Influenza in Osler's Modern Medicine, points out that acute anterior poliomyelitis can follow an attack of influenza. Brorstrem[82] (1910) noted the simultaneous occurrence of acute infantile paralysis and influenza in the Swedish County Tingeryd in 1905, 1906 and 1907, and in the spring of 1908. He maintained that infantile paralysis

and influenza are the same. Hiller[83] (1922) noted an increased incidence of poliomyelitis cases during an influenza epidemic and Chalier[84] (1942) observed an epidemic of poliomyelitis cases following one of influenza.

According to the older writers, poliomyelitis was not infrequently preceded by diarrhea; "foul bowels" was often mentioned as a factor. Osler and McCrae[58] state: "An interesting sequel of dysentery is paralysis. Woodward reported eight cases. Weir Mitchell mentions it as not uncommon, occurring chiefly in the form of paraplegia." Francis[85] (1917), of the Cook County Contagious Disease Hospital, Chicago, was able during an epidemic of poliomyelitis to produce a paralytic condition in rabbits resembling poliomyelitis by the injection of the Shiga dysentery bacillius. Doerr and Seidenberg[86] (1936) found that the dysentery toxin acts on the cecum and the lumbar and cervical enlargements of the spinal cord in the rabbit regardless of how it is introduced. De Teyssiew[87] (1921) reported acute poliomyelitis following the injection of anticholera vaccine.

Cholera infantum, also known as intoxication, toxicosis, infectious diarrhea, and summer complaint, not infrequently resulted in paralysis. In a series of 350 cases of poliomyelitis reported by Sinkler[88] (1890), twelve followed cholera infantum. This disease was attributed to bacterial toxins in food or in the intestinal tract as a result of heat and humidity in the summer and autumn. Potter[89] (1887) attributed the cause of cholera infantum to alkaloids in the food. He pointed out that there are five poisonous alkaloids that bear a relation to summer diarrhea, i.e., neurine, muscarine, choline, mydalein and a substance of undetermined position. The action of the first three of these he states is identical; the most important symptoms produced by a fatal dose are salivation, vomiting and diarrhea, dyspnea, paralysis and death.

Corresponding with this disease of infants, the cholera morbus of older children was characterized by vomiting and diarrhea; it was not infrequently followed by paralysis. Cholera morbus was attributed to fermentative changes in the ingesta. Both cholera infantum and cholera morbus showed exacerbations with hot weather, reaching their peak in "dog day" weather and ameliorating with the advent of cooler weather which corresponds with the poliomyelitis of today.

Malarial paralysis has been reported by a number of writers. Sterian[90] (1897) described a case of acute anterior poliomyelitis of malarial origin in an adult.

Bassette[37] (1892) reported a case, a five-year-old child, with paralysis of the left leg following mumps. She considered this case one of probable neuritis and poliomyelitis. Missimilly[91] (1913) reported a case of poliomyelitis following mumps in which there was complete flaccid paralysis and loss of reflexes. There was recovery with the exception of the left thigh muscles which became atrophied, and the nerves showed a reaction of degeneration.

Kilham et al.[92] (1949) point out that in 1948, in Massachusetts, there was an unusual incidence of mumps between June and November and at the same time there was an appreciable increase in poliomyelitis cases. They felt that many of the cases of non-paralytic poliomyelitis that were reported were probably cases of mumps meningoencephalitis. They found that 6 of 17 hospitalized patients, diagnosed clinically as nonparalytic poliomyelitis, were actually caused by mumps in which the salivary gland involvement was not evident.

Van Bogaert [93] (1909-10) reported an epidemic of poliomyelitis superimposed on or complicating a severe epidemic of measles. Moser[94] (1912) mentions meningitis, encephalitis and poliomyelitis as sequelae of measles. Osler and McCrae[58] (1923) point out that polyneuritis with widespread atrophy may occur as a complication of measles. Donlegny and Baixe[95] (1931) reported peracute polyneuritis of the bulbar type following measles. Panto[96] (1934) reported a case of flaccid paralysis ten days after the onset of measles in an infant of two years. Lafuente[97] (1943) pointed out that measles was considered to be the most frequent cause of paralysis in Mexican children.

Paralysis has been reported during the course of and following smallpox. Wilson and Ford[98] (1927) noted that clinical symptoms in general indicate an involvement of the anterior horn cells of the spinal cord. Some of the cases reported in the literature have presented the clinical appearance of acute ascending paralysis (Landry's paralysis) and some were cases of anterior poliomyelitis. In a case reported by Damaschino[99] (1860), a child two and one-half years old, had variola. During convalescence the lower limbs became weak. When examined six months later the affected

limbs were flaccid and had lost electrical contractility. At autopsy a focus of softening was found in the anterior part of the gray matter of the left side in the lumbar region of the spinal cord, and the nerve cells of the anterior horns were atrophied. The alteration in the cervical and thoracic regions were much less intense than in the lumbar region. In a case reported by Westphal[100] (1874), the gray matter of the cord was most affected and was infiltrated by fatty granular cells. Paralysis occurring in variola was reported in a man aged 20 years by Oettinger and Marinesco[101] (1895). Both gray and white matter of the lower thoracic region were affected but the gray more than the white. Perivascular infiltration of mononuclear and polymorphonuclear leukocytes were found in this portion of the spinal cord. Spiller[102] (1903) reported a case of anterior poliomyelitis during the course of smallpox in an adult and a case was reported also by Van Gehuchten[103] in the same year.

It was noted by Holt[11] and others, over fifty years ago, that poliomyelitis not infrequently followed anti-smallpox vaccination. In recent years there has been renewed interest in poliomyelitis following vaccinations and immunizations. Paul [104] reported a severe case of poliomyelitis following vaccination in 1928. Jeremburcz[105] (1930) reported two cases of poliomyelitis in connection with smallpox vaccination and in the same year Heidema[106] also made a similar report. In 1935, Banerjea[107] reported a case of poliomyelitis following vaccination of an infant for smallpox and, in 1940, Cervini and Tiscorma[108] reported the development of flaccid paralysis of the lower limbs ten days after smallpox vaccination in an 18-month-old child.

Attention was focused on the simultaneous occurrence of cases of postvaccinal neurological manifestations and poliomyelitis in England by Turnbull[109] as early as 1912, when he was investigating an epidemic of poliomyelitis. In 1923,[110] the issue of vaccine tubes began to rise that year about the middle of June, attaining its height in the last fortnight of July. Postvaccinal neurological manifestations appeared in the middle of June, reaching a maximum in the first half of August. The period of 1923, during which the majority of the postvaccinal cases occurred, was immediately antecedent to a rise of poliomyelitis and polioencephalitis. Following these observations in England, the association of vaccination with poliomyelitis and encephalomyelitis was noted in

the Netherlands, Czechoslovakia, Switzerland and other countries.

"Whooping cough, while less frequently than most other acute infectious diseases of childhood, is the forerunner of paralysis sometimes preceding its cerebral, spinal, and peripheral types."[37] Bassette[37] (1892) described a case of paralysis of the right leg in a 15-month-old child following whooping cough. Baginsky[111] (1911) speaks about the forms of paralysis in whooping cough, other than those caused by cerebral hemorrhages, that result from lesions in the brain or spinal cord. He reports a typical, ascending Landry's paralysis with rapid fatal termination in a boy of seven years of age occurring in connection with whooping cough. He states that there are individual cases of spastic spinal paralysis, of encephalitis with paraplegic symptoms, of multiple sclerosis with beginning bulbar symptoms and later a spastic paralytic condition, of polyneuritis with paraesthesia, anaesthesia and paralysis. Borrell[112] (1932) reported the development of a case of acute poliomyelitis in an infant with whooping cough.

It has been reported in recent years that whooping cough inoculations can be followed in some cases by the development of encephalomyelitis.[113-119] Coinciding with these observations, it has been noted in the past few years, and with increasing frequency since the original reports by Australian and British observers,[120-126] that poliomyelitis can also follow immunization against either or both whooping cough and diphtheria, as well as after immunization with the combined antigens of diphtheria, whooping cough and tetanus. The neurological reactions to these immunizing agents have been attributed to a toxic substance or a poison-like antigen formed by the immunizing agent which so affects the nervous system that paralysis results.

The administration of rabies vaccine is occasionally followed by paralysis of the dorsolumbar or Landry's paralysis type. These paralytic accidents have been attributed to the brain tissue substance in the offending material.

Two separate epizootics in animals of definitely established bacterial etiology which resulted in poliomyelitis, reported by Gard[127] (1944), appear to be of great significance. The first of these appeared in July 1941 when a number of young guinea pigs were bought and housed in the same stable room with a stock of mice. After two weeks some of the guinea pigs became ill

and within two months all of them died. It was found that the lymph nodes, especially the mesenteric glands, were enlarged and hyperemic. In cultures from mesenteric glands, salmonella enteritidis was constantly recovered, usually in pure culture. When this discovery was made the infection had already spread to the mice. During the height of the epizootic, the last week of August and the first week of September, four cases of poliomyelitis occurred in the mice. All four mice showed, besides the nervous system lesions, fatty degeneration of the liver and their mesenteric glands resembled those of the guinea pigs that were affected by the salmonella bacillus.

The second outbreak occurred in June 1943. As early as the middle of May an epizootic among stock mice had become evident affecting chiefly the young. At the height of the epizootic practically all young mice were attacked and most of them died. The initial symptoms consisted of a slimy or watery profuse diarrhea. The intestinal contents on culture yielded B. proteus vulgarus in some cases and by direct microscopy a large number of amebae, infusorians, and flagellates were observed. Adult mice, usually only females in the first week after delivery, when attacked were usually found dead without having displayed any obvious symptoms. Smears from the liver revealed the B. piliformis, and Gard considered this organism to be the cause of the epizootic. During the outbreak five cases of poliomyelitis developed among the mice.

COMMON DENOMINATORS OF CAUSE AND EFFECT

Sporadic cases of poliomyelitis may occur during any season of the year but epidemics occur particularly during hot weather when absolute humidity is high. Armstrong[128] (1951) found that poliomyelitis is most prevalent while the relative humidity level is above 28 per cent and the temperature above 90° F. Corresponding with these observations is the lesser known fact that poisons and toxins may produce clinical neurological manifestations more frequently in hot weather than during other seasons of the year. Lead,[129-133] for example, which has been described as one cause of poliomyelitis is an outstanding example.

Suzuki and Kaneko[134] (1924), as well as Fukushima and Matsumato[135] (1928), noted a seasonal incidence of lead poisoning. Blackman[136] (1937) demonstrated the onset of lead encephalitis

in 19 of 22 cases between the months of June and October. Rappaport and Rubin[137] (1941) observed the manifestations of lead encephalopathy between the months of May and September. Giannattasio et al.[138] (1951) reported fourteen cases of lead poisoning in children, 12 of which occurred between June 1951 and September 1951.

Blackman[136] suggested that this seasonal incidence of lead poisoning may be due to precipitation of the central nervous system lesions by factors which cause vasodilatation, such as fever and the heat of the summer and early fall months. Rappaport and Rubin[137] suggested that sensitization by sunlight of increased amounts of porphyrin in plumbism may contribute to the seasonal incidence.

This reference to porphyrin in plumbism is important inasmuch as it has been demonstrated that coproporphyrin III is present in the urine of experimental and clinical lead poisoning, as well as in poisonings by other substances. Analogous urinary findings of coproporphyrin III have been observed in cases of poliomyelitis by Watson et al.[139, 140] (1947). Salter[141] (1952) points out in his Textbook of Pharmacology that the porphyrins are of interest because they bear witness to a derangement in metabolism which usually reflects the presence of some other poison.

That the atmospheric and climatic conditions of the summer and fall are responsible for the development of neurological complications and sequelae in infectious diseases, and following vaccination and other immunological procedures, is apparent from the facts that have already been considered in this paper. The question naturally arises, "Does a toxin produced by an infectious disease organism as well as an antigen contained in immunizing agents become neurotrophic when atmospheric and climatic conditions are favorable." The observation by Gard,[127] that the poliomyelitis which resulted from the salmonella enterides infections in mice between July and September 1941, and the B. piliformis infections that resulted in mouse poliomyelitis in the summer of 1943, as well as the recent observations that vaccinations and other immunizing procedures during the summer are followed sometimes by poliomyelitis, strongly suggest this possibility.

Other facts must be considered in explaining some cases of poliomyelitis. For example, the poliomyelitis epidemic season,

May to September or October, corresponds with the growth and harvest of perishable fruits and vegetables. During this period drought conditions favor the development of intrinsic poisons in plants and the increased use of poisonous insecticides which for some individuals may have a neurotrophic effect.

It is a well-known fact that fatigue is an important factor in precipitating an attack of poliomyelitis. A similar physiological alteration of the body will bring about the neurological manifestations of poisoning by lead and other poisons. A similar situation seems to exist in relation to trauma, chilling, operations, pregnancy, etc. in poliomyelitis and various forms of poisoning.

There is evidence that a disturbance in the biochemistry of the nervous tissues occurs both in poliomyelitis and poisoning. In other words, some enzyme system of the central nervous system concerned with the synthesis of some essential structure of the cell appears to be affected in each case. In the complex physiological and biochemical cycles of the nerve cell, there are several enzymatic systems intimately interrelated, a disturbance of any one of which might disrupt the function of the cell as an organized unit. The end result is the same, i.e. motor neurone injury or destruction. That the mode of action of the various etiological agents capable of producing poliomyelitis is at least similar if not identical, is suggested by the similarity of the resulting lesion.

SUMMARY

1. In the absence of a specific diagnostic test for poliomyelitis, the diagnosis of the vast majority of cases has been dependent merely on personal judgement.

2. There is evidence that poliomyelitis has many causes rather than a single cause.

3. Common denominators of cause and effect in all cases appear to depend on seasonal and climatic conditions, fatigue, trauma, etc., and disturbances of the physiology and chemistry of the nerve cell.

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